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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SINGH, SATYENDRA K	
ART UNIT	PAPER NUMBER
1657	
MAIL DATE	DELIVERY MODE
08/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,811	EDENS ET AL.	
	Examiner	Art Unit	
	SATYENDRA K. SINGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 18-22* is/are pending in the application.

4a) Of the above claim(s) *1-8,13-15 and 18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/22/06; 7/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response (and amendments to claims) filed on 06/01/2009 is duly acknowledged.

Claims 1-15 and 18-22 are pending in this application.

Claims 16 and 17 have been canceled by applicants.

Election/Restrictions

Applicant's election with traverse of **group V** (claims 9-12; directed to a method of using proline specific endoprotease, as recited in claim 9, as currently amended; elected specie of disease being **"celiac disease"**) in the reply filed on 06/01/09 is acknowledged. The traversal is on the ground(s) that "*Notwithstanding the above election, reconsideration of the restriction requirement is requested because examination of all pending claims* ***would not constitute a serious burden****. Although the inventions identified by the Examiner are separately patentable..... they should be examined because they are generic for the elected invention. In this respect, diseases associated with the occurrence of celiac disease are generic for "celiac disease" itself*". This is not found persuasive because burden lies not only in the search of US Patents, but in the search for literature and foreign patents and examination of the claim language and specification for compliance with the statutes concerning new matter, distinctness, scope of enablement, and double patenting issues.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8, 13-15, and 18-22 have been withdrawn as being directed to non-elected inventions.

Claims 9-12 (invention of group V, elected specie "celiac disease") have been examined on their merits in this office action.

NOTE: Claims 9-12 have been interpreted as generally directed to **a method of treatment** of patients in need thereof or patients suffering from "celiac disease", wherein the method requires oral (ingestion route) administration of a dietary supplement comprising a proline specific endoprotease having characteristics as recited in claims 9-12.

Specification

The disclosure is **objected to** because it contains an **embedded hyperlink** and/or other form of browser-executable code on **page 11** of instant specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names **joint inventors**. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Messer et al (1976; IDS, citation UR) in view of Hausch et al (2002; [U]) and Dekker et al (WO 02/45524 A2; [N]).

Claims 9-12 have been interpreted as generally directed to **a method of treatment of patients in need thereof or patients suffering from celiac disease** (elected specie), wherein the method requires oral (ingestion route) administration of a dietary supplement comprising a proline specific endoprotease (obtained from an *Aspergillus* sp.; that can hydrolyze proline-rich peptides that are associated with celiac disease at a pH of below 5.5, or that has a pH optimum below 6.5; see specific recitations of claims 9-12).

Messer et al (IDS) disclose a method of treatment of patients in need thereof or patients suffering from celiac disease, wherein the patients are orally administered a dietary formulation or supplement comprising a digestive enzyme (i.e. oral enzyme therapy to treat celiac disease; see entire report at page 1022) such as papain (in the form of enteric-coated tablets of commercially available papain) in order to help destroy the gluten to improve response to gluten free diet in the patients suffering from celiac disease, wherein based on their experimental results, they recommend oral, crude papain enzyme administration as an adjunct treatment to gluten-free diet in the treatment of gluten intolerance in patients in need thereof.

However, Messer et al do not use "**proline specific endoprotease**" as required by the instant claims 9-12.

Hausch et al [U] disclose the immunodominant gliadin peptides that are now known to be the cause of celiac disease or gluten intolerance, and they show that these peptides are exceptionally resistant to enzymatic digestion in patients with such disorders as celiac disease (see abstract, and introduction, in particular). They also disclose the fact, that a trace amounts of exogenously added (both, *in vitro* or *ex vivo*) prolyl endopeptidase (albeit from a bacterial source) was able to efficiently destroy or digest said immunodominant peptides, suggesting "a possible enzyme therapy strategy for celiac sprue..." (see abstract, page G996, in particular). Hausch et al also state that "*...therefore, we suggest that supplementation of the celiac diet with bioavailable PEP, with or without DPP IV and DCP I, by virtue of facilitating gliadin peptide cleavage to nontoxic and/or digestible fragments may be useful in attenuating or perhaps even eliminating the inflammatory response to gluten. Such a strategy would be analogous to the enzyme therapy treatment in the case of lactose intolerance, where orally administered lactase is effective in cleaving and thereby detoxifying the lactose in milk product*" (see page G1002, left column, and references contained therein)

Therefore, given the detailed disclosure by the cited prior art references of record, at the time this invention was made, it would have been obvious to a person of ordinary skill in the art to modify the method of treatment disclosed by Messer et al such that it uses a dietary supplement comprising proly endopeptidase as explicitly suggested and motivated by the disclosure of Hausch et al. Since, Hausch et al clearly demonstrated the use of proly endopeptidase in destroying the immunogenic gluten peptides that are known to be the root cause of the inflammatory response in patients

with celiac disease, an artisan of ordinary skill in the art would be motivated to substitute the enzyme, papain with proly endopeptidase of Hausch et al in order to successfully destroy the gliadin peptides, and thus achieve a superior and effective method of treatment of patients in need thereof.

However, the combined teachings of Messer et al and Hausch et al do not explicitly disclose the use of a proline endoprotease that has the hydrolytic activity at **pH below 5.5, or a pH optimum of below 6.5**, and that is obtained from an ***Aspergillus* sp.**

Dekker et al [N] disclose such an enzyme (a proline endoprotease that can hydrolyze proline-rich peptides that are associated with celiac disease at a pH of below 5.5, or that has a pH optimum below 6.5, and that has been derived from *Aspergillus* sp.) that can be used for digesting or hydrolyzing various types of proteins and peptides to obtain hydrolysates that can be used in various applications, including allergen free diets for babies, and for obtaining wheat gluten hydrolysates which are normally difficult to obtain (see Dekker et al, pages 3, 8 and 11, in particular) as it is poorly soluble at acidic pH. They disclose the extensive usefulness and application of this enzyme that acts in acidic conditions with a pH optimum below 6.5 (preferably pH 3.5 to 6.5), and that can be used to digest wheat gluten from barley into digestible peptides in order to protect gastric mucosa, which is normally at acidic pH.

Thus, given the disclosure from Dekker et al for a suitable prolyl endoprotease (derived from *Aspergillus* sp.) that can work best under the acidic pH conditions (such as of stomach and/or intestine of patients), an artisan of ordinary skill in the art would

have been motivated to substitute a better prolyl endoprotease enzyme, albeit from an *Aspergillus* sp., as explicitly taught by the referenced invention of Dekker et al in order to achieve a superior method of treatment of patients suffering from celiac disease with a reasonable expectation of success, as evidenced by the detailed disclosure of Dekker et al that demonstrate the efficient digestion of various types of proteins using said prolyl endoprotease having an acidic pH optimum, which will be suitable for the enzyme therapy (in the method of Messer et al and Hausch et al) as an oral dietary supplement.

Thus, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill in the art, at the time the claimed invention was made.

As per MPEP 2111.01, *during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination the USPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz*, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

Conclusion

NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SATYENDRA K. SINGH whose telephone number is (571)272-8790. The examiner can normally be reached on 9-5MF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sandra Saucier/

Primary Examiner, Art Unit 1651

/Satyendra K. Singh/
Examiner, Art Unit 1657